



Robert F. Gertenbach, President The Council for Tobacco Research, U.S.A., Inc. 900 Third Ave., NEW YORK, NY 10022

Dear Dr. Gertenbach,

This letter represents an informal request as to whether The Council for Tobacco Research may wish to receive a full proposal for some basic research we hope to pursue.

My laboratory works on the function and biochemistry of blood platelets and we are particularly interested in the mechanisms of platelet activation and how overall function is regulated. An exciting avenue of research has recently developed where the efficiency of platelet aggregation and adhesion is powerfully controlled by changes in the amount of cyclic GMP. An apparent paradox has arisen in that compounds present in cigarette smoke, such as carbon monoxide, can strongly inhibit platelet function. Sodium nitroprusside has a similar effect and both agents increase levels of cyclic GMP. However, other compounds such as epinephrine or atrial natriuretic peptide, both associated with high blood pressure, can directly cause platelet activation, or powerfully potentiate it. These agents also raise levels of platelet cyclic GMP.

Our proposed research is directed to this paradox. We wish to understand the basic mechanisms leading to the synthesis of cyclic GMP and how the opposing effects on platelet function can be rationalized. The role of cyclic GMP in regulating cell function therefore has relevance to platelet involvement in atherosclerosis.

We look forward to learning whether you would be interested in supporting this type of research and would be happy to provide any further information at this stage.

Yours sincerely,

Adrian R.L. Gear, D.Phil. Professor of Biochemistry